The 11-year functional outcome of bipolar and major depressive disorders in Butajira, Ethiopia

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ABSTRACT

Background: Long-term follow up studies of functioning in people with bipolar (type I) and major depressive disorders (BD and MDD) have not been reported from Africa.
Objectives: To describe the long-term functional outcome of BD and MDD, and factors that influence such outcome.
Methods: Door-to-door survey of 83,282 adults (ages 15–49 years) in a rural district of Ethiopia to identify potential cases whose diagnosis was later confirmed by standardized clinician interviews were followed by for an average of 11 years. The Short-Form- SF-36 scale was used to describe the functional outcome. Mixed linear models were used to evaluate potential factors associated with outcome. A total of 311 people with BD and 187 people with MDD that were identified at baseline and with complete data on functional outcome were included in the analyses.
Results: Mean social functioning levels at baseline were 55–65% for people with BD and 55% for MDD but improved with follow-up. About 33% incident and 37% prevalent cases of people with BD had reduced social functioning for three years or more. Baseline functioning was significantly associated with longitudinal functioning. When baseline functioning is adjusted in the model, longitudinal functioning was not associated with socio-demographic or illness characteristics.
Conclusions: The level of functions of people with BP and MDD were significantly lower than that of the general population both at baseline and during the follow-up period. Although there were improvements in function with follow-up, a significant proportion had functional deficits during the follow-up period.

1. Introduction

There has been a shift in mental health services from an emphasis on treatment focused on reducing symptoms to an approach which takes into consideration both well-being and functioning (Brazier et al.,

2014). Bipolar disorder (BD) is the 16th leading cause of disability in the world responsible for the loss of more disability-adjusted life years than cancer, ischemic heart disease and major neurologic conditions (Ferrari et al., 2016), primarily because of its early onset and chronicity across the lifespan. Many long-term studies of functional outcome have

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been reported from developed countries (Dean, Gerner, & Gerner, 2004; Gitlin & Miklowitz, 2017; Goodwin, 2000). However, relatively few studies have been reported from developing countries (Brown et al., 1998; Dube, Kumar, & Dube, 1984; Khanna, Gupta, & Shanker, 1992; Rao & Nammalvar, 1977; Thomas, Nisha, & Varghese, 2016; Topuzoğlu et al., 2015), and none from sub-Saharan Africa.

Major depressive disorder (MDD) is expected to be the leading cause of years of disability in 2030 (Ferrari, Charlson, Norman, Patten, & Freedman, 2013). In addition to being a prevalent and chronic disorder, the level of functional impairment in MDD is as high as, or even higher than, chronic diseases, including cardiovascular disorders (Moussavi et al., 2007). The impairment continues even during remission from clinical symptoms (Verduijn et al., 2017). The functional outcome of MDD has been extensively studied in the developed world and to a lesser extent in developing countries as some recent reviews show (Sheehana, Nakagomeb, Asamic, Papadopoulos, & Boucher, 2017). However, because of the scarcity of long-term studies, the functional outcome of MDD in Africa is not known.

We have earlier reported (Kebede et al., 2005; Kebede, Alem, Shibire Deyassa, Negash, & Beyero, 2006) the short-term functional outcome of BD from the Butajira follow up study of severe mental disorders that was initiated in 1998. The study was unique in that people with BP and MDD: (a) were recruited from a defined community instead of clinics, (b) had not had any medical treatment at baseline (over 97%), and (c) were followed for an average of 11 years to sufficiently allow assessment of long-term outcome. The present study describes the long-term functional outcomes of people with BD and MDD and factors that influence such outcomes.

2. Methods

The details of the methods that were followed have been described elsewhere (Fekadu et al., 2015; Kebede et al., 2003; Shibre et al., 2014; Shibre et al., 2015), but are briefly described here. The Butajira follow up study on severe mental disorders was initiated in 1998 with a door-to-door survey of the district adult (ages 15–49 years) population estimated at 83,282. The psychoses and affective disorder modules of the Composite International Diagnostic Interview (CIDI) were used as a screening instrument to identify potential cases of severe mental disorders and was used to interview 68,378 individuals. The average non-response rate was more in rural areas (18.7%) than in the town (13.6%). Being out of the district on a business trip accounted for 65% of the non-response. In addition to the survey, key informants (KI) were used to identify individuals with probable severe mental illnesses. The performance of the CIDI and KI methods in identifying people with schizophrenia and affective disorders has been reported earlier (Shibre et al., 2002).

In the second stage, those that tested positive for psychoses and affective disorders on the CIDI and those identified by key informants underwent evaluation by physicians using the Amharic version of the Schedule for Clinical Assessment in Neuropsychiatry (SCAN) (Wing, 1996; Wing et al., 1989). A total of 2166 individuals was identified as probable cases of schizophrenia or affective disorders by the CIDI interview. Of these, 1738 (80.5%) volunteered for the SCAN interview. The key informants identified a total of 719 probable cases of severe mental disorder. Of these, 547 (76.1%) subsequently underwent evaluation by the SCAN. A total of 2285 SCAN interviews was undertaken (79% of the total 2878 potential cases identified both by the CIDI interview and key informants).

Out of the 2285 SCAN interviewed persons, 847 were diagnosed as having severe mental disorders (schizophrenia, BD or MDD) according to ICD-10 criteria. During the follow-up study, a total of 75 additional incident cases were diagnosed using the SCAN, bringing the total to 919. Of these, a total of 345 people with BD and 215 with MDD were identified initially. The present study focused on individuals with BD (311) and MDD (187) with complete outcome data which met the

following inclusion criteria. (a) Age between 15 and 49 years; (b) residence for at least six months in the area; and (c) evidence of the presence of BD (ICD-10 designation: F30, F31) and MDD (ICD-10 designation: F32, F33) after a comprehensive assessment using the SCAN. People with bipolar II disorder were not included.

People with severe mental disorders were scheduled for yearly follow-up evaluations after the baseline assessment, using the same instruments. Psychiatric nurses trained in its use administered the Short Form 36 (SF-36), which was used to quantify physical and social functional outcomes. The SF-36 is widely used for measuring outcomes of both physical and mental illnesses and has been shown to validly measure functioning and health-related quality of life (Brazier et al., 1992). The instrument has also demonstrated good internal consistency, stability, and concurrent validity in people with BD (Leidy, Palmer, Murray, Robb, & Revicki, 1998). The Amharic version that was used in this study has also demonstrated good reliability and validity in the general population of Butajira (Kebede et al., 2004). The SF-36 instrument includes 36 items that yield eight domains (or scales) when scored. The physical functioning domain (PF, ten items) assesses limitations in physical activities, such as walking and climbing due to health problems. The social functioning domain (SF, two items) assesses limitation in social activities because of physical and emotional problems. Higher SF-36 scores represent higher levels of function. We used SF and PF to measure functioning.

Clinical course and outcome data were collected using the Longitudinal Interval Follow-up Evaluation (LIFE) chart (Keller et al., 1987). The LIFE chart is a semi-structured questionnaire suitable for summarizing longitudinal data. Four psychiatrists who were trained for four days administered the LIFE chart. The key rating tool in the LIFE chart is the Psychiatric Status Rating (PSR). The PSR is a six-point symptom severity rating, ranging from one to six. A rating of one indicates the absence of symptoms while a rating of six is consistent with severe symptoms. The PSR ratings were completed using all available information: reports by patients and family, the monthly clinical records, annual symptomatic and functional ratings, reports from psychiatric nurses, and reports from the project outreach workers who had monthly contacts with the people with severe mental disorders and their families. When participants were unable to attend the psychiatric clinic for the final assessment, raters visited the person's house with their permission.

We conducted a stratified analysis and presented the results of our study separately for 70 incident cases of BP with the onset of recognizable illness within the last two years before recruitment into the study, and for 241 prevalent cases with onset of illness of three or more years. For MDD, 41 incident and 146 prevalent cases were analyzed, to describe the outcome in two different stages of illness, and also to limit the selection bias that could arise from the use of varying proportions of chronic cases (Eaton, 1995).

A SAS-based SF-36 scoring algorithm (Ware, 1993) supplied by the developers of the instrument was used to calculate individual scores. IBM SPSS (version 19) was used for univariate, bivariate and multivariate analyses. To evaluate potential predictors of outcome we employed linear random coefficient models. These models are superior to others in investigating individual change because they provide more flexibility in examining situations where there may be missing data and unequally spaced time intervals, which is the case with the present study (Heck, Thomas, & Tabata, 2011; Hennen, 2003). We fitted separate models for each of the two outcomes evaluated (yearly PF and SF scores) as dependent variables. As independent variables, the following were evaluated using the models. (a) sociodemographic characteristics: sex, age, marital status, literacy, urban-rural residence, religion; (b) illness characteristics: age of onset, speed of onset, duration of illness, history of medical treatment at baseline, medication adherence, and substance use; (c) year of follow-up; (d) annual PSR scores; and, (e) baseline SF and PF scores. Maximum likelihood estimations were used to fit the random coefficient models to the data.

The study was approved by the ethical review committees of both the Department of Community Health and the Faculty of Medicine, Addis Ababa University. The study has made possible the establishment of a mental health service in the district. The people identified with BD or MDD were offered psychiatric treatment as appropriate, free of charge and this has continued until the present.

3. Results

A total of 311 people with BD and 187 people with MDD that were identified at baseline and with complete data on functional outcome were included in the analyses. There were 70 incident cases of BD and 41 incident cases of MDD (Fig. 1). For BD, the mean age was 29 years, and 46% were females, 65% were married, and 84% resided in rural areas. The mean duration of education was two years, and the group was followed for a mean of 11 years (Table 1). The corresponding figure for MDD is shown in Table 2. The mean age was 32 years, 62% were females, 71% were married, and 81% resided in rural areas. They were educated for a mean of two years and were followed for a mean of 11 years.

Mean social functioning levels were low at baseline for both people with BD (55–65%) and MDD (55%) but improved with follow-up. In both BD and MDD, there were progressive increase in the SF-36 social functioning (SF) scores (i.e., the trend of improvement) for most of the follow-up period (Figs. 2 and 3). The level and pattern of improvement were similar between the incident and prevalent cases. However, the scores for both incident and prevalent cases were lower than the population means for most of the follow-up period. This gap was statistically significant until the 6th year of follow-up. Beyond this year there was an overlap of the 95% confidence limits of the mean values between the study and the general population. There was no marked improvement in the progression of physical function (PF) scores, nor any significant gap between the PF scores of the cohort and the general population.

A third of incident (33%) and prevalent cases (37%) of BD had reduced social functioning for three years or more (Fig. 3). The corresponding percentages for physical function were 17% for the incident and 28% for prevalent cases. For MDD about half of the incident (46%) and prevalent (49%) cases had reduced social function for three years or more (Fig. 4). About one-fifth of incident cases and 35% of prevalent cases of MDD had reduced physical function for three years or more (Fig. 5).

The trend in the improvement of the social functioning of people with BD during the follow-up period was statistically significant (P < 0.001) for both incident and prevalent cases (Table 3). The trend in the improvements of the physical functioning of the incident and prevalent cases were also statistically significant (P < 0.001, not shown in the Table). SF scores increased significantly in the incident (P = 0.001) and prevalent (P < 0.001) cases of MDD (Table 4). The increase in PF scores was not statistically significant (not shown) (Fig. 5).

Baseline levels of social functioning of people with BD were significantly associated with improving trend of social functioning during the follow-up period in both incident and prevalent cases (P < 0.001). Both follow-up PSR (i.e., symptom severity) scores for mania and depression were not significantly associated with improvement in social functioning. Sex, religion, rural residence, the age of onset, the speed of onset, duration of illness, history of use of neuroleptic treatment before recruitment, and substance use (alcohol, tobacco, and khat[1]) were not associated with social functioning. Similarly, baseline physical functioning was significantly associated with improving trend of physical

functioning during the follow-up period. None of the other factors included were significantly associated with improvement of physical functioning (not shown).

Baseline levels of social functioning were significantly associated (P < 0.001) with improving trend of social functioning of both incident and prevalent cases of MDD during the follow-up period (Table 4). The association between follow-up PSR scores and improvement in social functioning were not significant. None of the demographic or illness characteristics included in the model were significantly associated with improvement of social functioning. A similar pattern of significant association of follow-up PF with baseline PF (P < 0.001) was observed, but this was not the case for follow-up PSR or any of the demographic or illness characteristics included in the model (not shown).

4. Discussion

The results show poor social and, to a lesser extent, physical functioning at baseline, that improved with follow-up of people with BD and MDD. However, the level of functioning of a third of the people with BD and half of the people with MDD was below the norm for the general population for most of the follow-up period. Baseline functioning was a predictor of long-term functioning in both BD and MDD. When baseline functioning was adjusted for, the long-term functioning of either the people with BD nor MDD was associated with several socio-demographic and illness characteristics.

We have attempted to limit the influence of several potential confounders, selection bias and other methodological problems that affected several other outcome studies (Keck et al., 1998; MacQueen, Young, & Joffe, 2001). Specifically, the participants were recruited from a defined community, they were predominantly (93%) neuroleptic naive at baseline (Negash et al., 2005), and were followed over an extended period to assess long-term outcome. We have employed widely acceptable and standardized diagnostic classification methods and data collection tools to identify and classify cases and to measure both outcomes and potential predictors (Eaton, 1995). We have also stratified our analysis by the incident and prevalent cases to limit selection bias and used random mixed linear models to adjust for potential confounders in assessing predictors of functional outcome (Hennen, 2003).

Social functioning was markedly lower than that of the general population in both BD and MDD at baseline and at all subsequent years of follow-up indicating a high level of residual disability. We have assumed that the level of functioning of the general population remained constant during the follow-up period. Although variation in the level of functioning of the general population is to be expected, it is unlikely that any variation will be large. Very few studies had compared their cases' long-term functioning with that of the general population. Gutierrez-Rojas et al. (2008) and ten Doesschate, Koeter, Bockting, Schene, and The DELTA Study Group (2010) have shown that functioning of people with BD and recurrent MDD were markedly lower than that of the population norm. A comparison of people with and without BD and MDD has also shown similar results during a 3-year follow-up in another study (Rhebergen et al., 2010). A review of studies on BD (MacQueen et al., 2001) has shown that 30–60% had detectable levels of psychosocial impairment during follow-up. Our findings also lie within these ranges.

We have also shown that a substantial proportion of people with BD (about a third) and MDD (about half) had reduced function for three years or more, showing the chronicity of both disorders. Other studies have reported that the proportion of time impaired between 30% and 40% as reviewed by Sanchez-Moreno et al. (2009). The NIMH Collaborative Depression Study has also reported 54 to 59% of follow-up time impaired in people with BD and MDD followed for an average of 18 years (Judd et al., 2008). Analysis of pooled data from 25 studies of 3936 people with BD and 6415 with MDD followed for over nine years

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[1] Khat is a flowering plant (Catha edulis), the leaves of which are chewed for their stimulant and appetite-suppressing effect. The leaves contain cathinone, which is an amphetamine-like molecule.
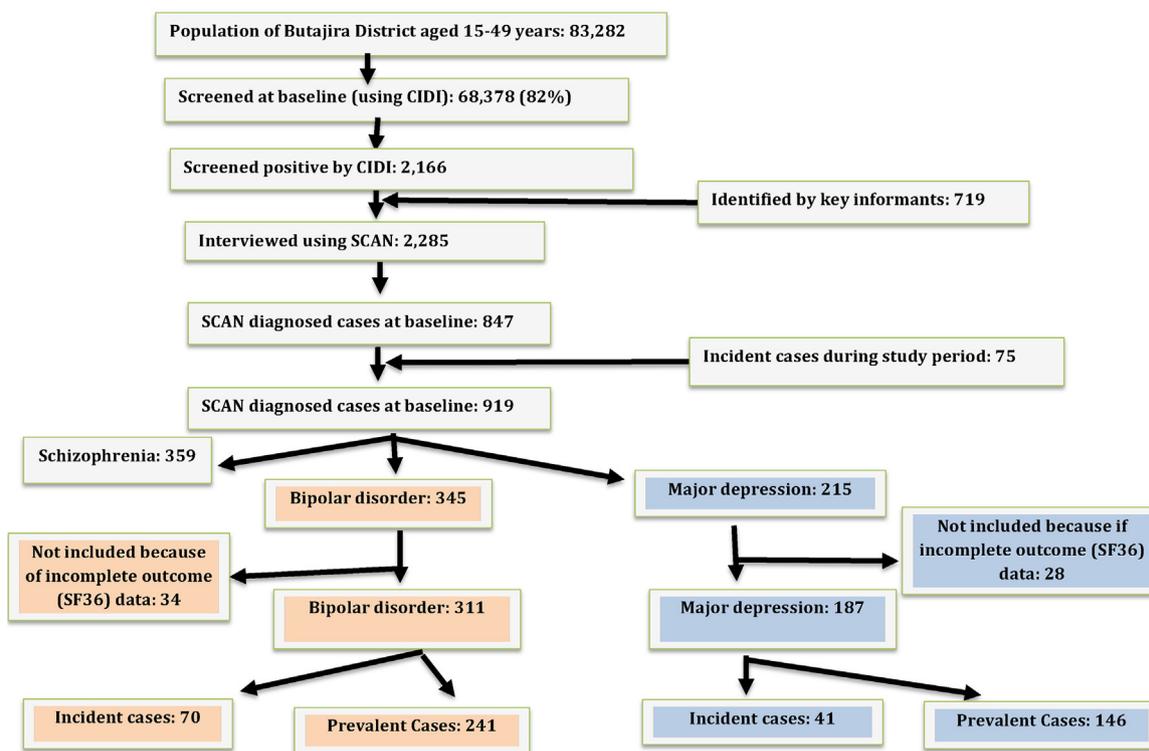
Fig. 1. Flow diagram of the follow-up study of people with bipolar disorder and major depression in Butajira, Ethiopia.

Table 1
Baseline characteristics of people with bipolar disorder in the Butajira follow-up study, Ethiopia.

		Incident cases[*]		Prevalent cases		All cases	
		Number	Percent	Number	Percent	Number	Percent
Sex	Female	30	42.9	113	46.9	143	46.0
	Male	40	57.1	128	53.1	168	54.0
Religion	Muslim	52	74.3	164	68.0	216	69.5
	Christian	18	25.7	77	32.0	95	30.5
Marital status	Married	32	45.7	168	70.3	200	64.7
	Others	38	54.3	71	29.7	109	35.3
Residence	Urban	8	11.4	42	17.4	50	16.1
	Rural	62	88.6	199	82.6	261	83.9
Speed of onset	Acute[**]	60	85.7	206	95.4	262	94.9
	Insidious	10	14.3	10	4.6	14	5.1
History of medical treatment at baseline	None	58	98.3	195	97.5	253	97.7
	Other	1	1.7	5	2.5	6	2.3
Medication adherence	75% or less	53	76.8	146	60.6	199	64.2
	> 75%	16	23.2	95	39.4	111	35.8
Substance use	No	62	88.6	214	88.8	276	88.7
	Yes	8	11.4	27	11.2	35	11.3
Total[***]		70	100.0	241	100.0	311	100.0

|		Mean	Standard error (SE)	Mean	SE	Mean	SE
Age	Years	24.2	.9	30.5	.5	29.1	.5
Education	Years	1.9	.4	2.2	.2	2.1	.2
Age of onset	Years	23.1	.9	21.3	.4	21.7	.4
Duration of illness at entry to study	Years	2.0	.8	9.6	.5	7.9	.4
Follow-up duration	Years	10.4	.3	10.9	.2	10.8	.1
Baseline physical functioning score[****]	Scale: 1–100	82.1	2.3	79.1	1.2	79.8	1.0
Baseline social functioning score[****]	Scale: 1–100	63.9	3.2	58.5	1.5	59.7	1.3
Baseline symptom severity score[*****]	Scale: 1–6	3.2	.3	2.2	.1	2.5	.1

* Incident cases are those with the onset of illness two years or less on entry to the study.

** Acute = onset within three months or less.

*** Missing values not shown. Sub-totals may vary.

**** Higher mean score values indicate higher functioning.

***** Higher mean score values indicate more severe symptoms.

Table 2
Baseline characteristics of the people with major depressive disorder in the Butajira follow-up study, Ethiopia.

		Incident cases[*]		Prevalent cases		All cases	
		Number	Percent	Number	Percent	Number	Percent
Sex	Female	22	53.7	93	63.7	115	61.5
	Male	19	46.3	53	36.3	72	38.5
Religion	Muslim	30	73.2	97	66.4	127	67.9
	Christian	11	26.8	49	33.6	60	32.1
Marital status	Married	24	60.0	106	73.6	130	70.7
	Others	16	40.0	38	26.4	54	29.3
Residence	Urban	12	29.3	24	16.4	36	19.3
	Rural	29	70.7	122	83.6	151	80.7
Speed of onset[**]	Acute	27	81.8	120	88.2	147	87.0
	Insidious	6	18.2	16	11.8	22	13.0
History of medical treatment at baseline	None	34	97.1	135	98.5	169	98.3
	Other	1	2.9	2	1.5	3	1.7
Medication adherence	75% or less	29	70.7	11	57.9	138	73.8
	> 75%	12	29.3	8	42.1	49	26.2
Substance use	No	40	97.6	137	93.8	177	94.7
	Yes	1	2.4	9	6.2	10	5.3
Total[***]		41	100.0	146	100.0	187	100.0
		Mean	Standard error (SE)	Mean	SE	Mean	SE
Age	Years	28.7	1.4	33.1	.7	32.1	.7
Education	Years	2.5	.5	1.9	.3	2.1	.3
Age of onset	Years	27.7	1.5	26.5	.7	26.8	.6
Duration of illness at entry to study	Years	1.1	.1	8.1	.7	6.5	.6
Follow-up duration	Years	10.5	.4	11.1	.2	11.0	.2
Baseline physical functioning score[****]	Scale: 1–100	79.9	3.6	77.7	1.5	78.2	1.4
Baseline social functioning score[****]	Scale: 1–100	56.1	3.2	57.8	1.9	57.4	1.6
Baseline symptom severity score[*****]	Scale: 1–6	4.2	.3	3.8	.2	3.9	.1

* Incident cases are those with the onset of illness two years or less on entry to the study.
** Acute = onset within three months or less.
*** Missing values not shown. Sub-totals may vary.
**** Higher mean score values indicate higher functioning.
***** Higher mean score values indicate more severe symptoms.
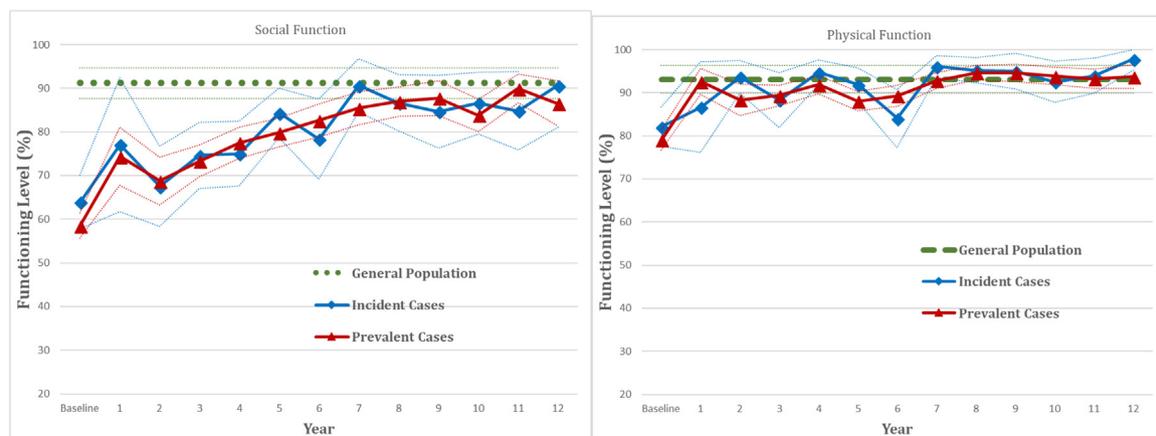
Fig. 2. Yearly trend in mean functioning level (%) of people with bipolar disorder* compared to the general population norm, Butajira, Ethiopia (the fine dotted lines represent 95% confidence limits).
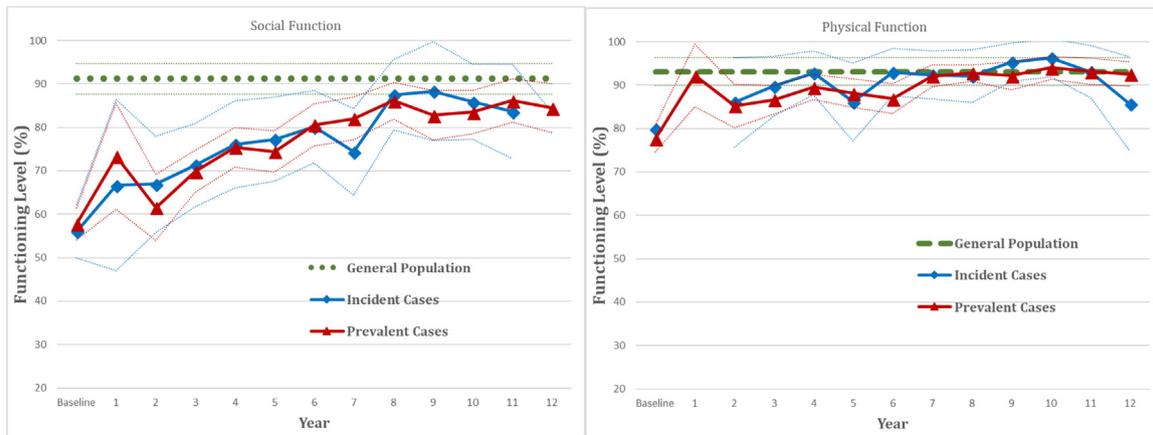* Incident cases (n = 70) are those with the onset of illness two years or less on entry to the study. The rest were categorized as prevalent cases (n = 241); Short Form Medical Outcome (SF-36) physical and social function scores were used as outcome measures. SF-36 score mean values are given on a scale of 1 to 100. Higher mean values indicate higher functioning; the fine dotted lines represent 95% confidence limits.

has shown that the proportions of time spent in illness were 44% for BD and 46% for MDD (Forte et al., 2015).

None of the socio-demographic factors considered in the present study were significantly associated with improved functioning in either people with BD or MDD. Comparison of our findings with what has been reported in the literature may be difficult because of methodological differences. However, our results are in accordance with the results of a recent systematic review and meta-analysis (Bortolato et al., 2017), which reported that 13 demographic factors (Education,

education of parents, ethnicity, gender, income, marital status, occupation, place of residence, SES, unemployment), and medication and substance use were not associated with functional outcome in people with BD.

None of the clinical characteristics considered in our study (age of onset, the speed of onset, duration of illness at entry, neuroleptic use at entry, substance use, or follow-up symptom severity score), were associated with functional outcome. Age of onset, duration of illness and type of onset may not be reported accurately in a population of low

Fig. 3. Yearly trend in mean functioning level (%) of people with major depressive disorder* compared to the general population norm, Butajira, Ethiopia (the fine dotted lines represent 95% confidence limits).

* Incident cases (*n* = 41) are those with the onset of illness two years or less on entry to the study. The rest were categorized as p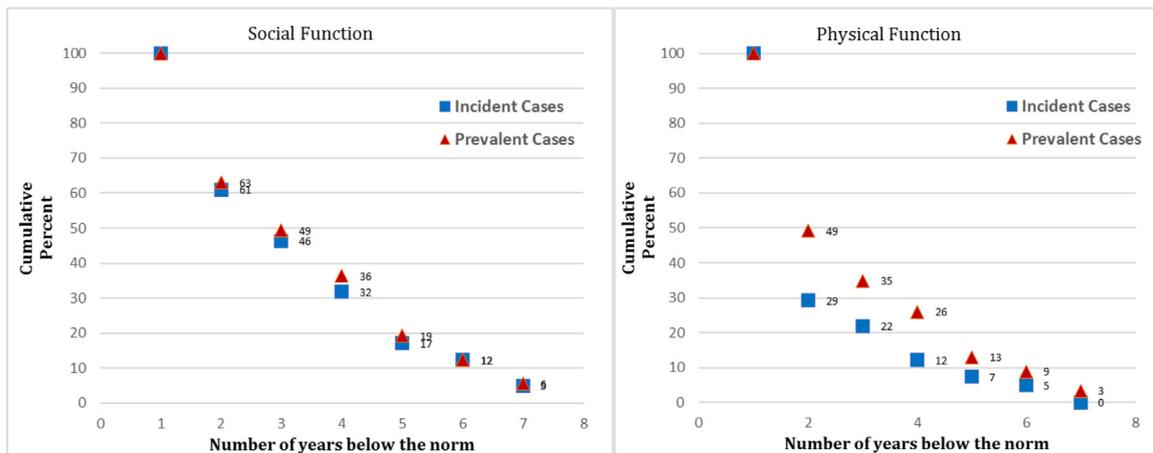revalent cases (*n* = 146); Short Form Medical Outcome (SF-36) physical and social function scores were used as outcome measures. SF-36 score mean values are given on a scale of 1 to 100. Higher mean values indicate higher functioning.
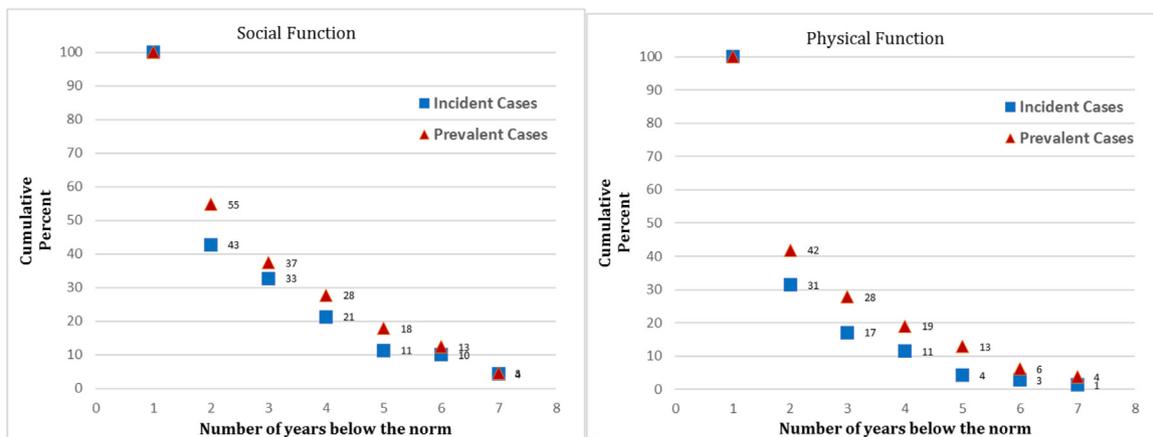
Fig. 4. Length of time in which people with bipolar disorder had reduced *social and physical functioning**, Butajira, Ethiopia.
* As compared with the population norm. For example: about a third (28%) of prevalent and one-fifth (21%) of incident cases had reduced social functioning for four years or more. Incident cases are those with the onset of illness two years or less on entry to the study.

Fig. 5. Length of time in which people with major depressive disorder had reduced *social and physical functioning**, Butajira, Ethiopia.
* Short Form Medical Outcome (SF-36) physical and social function scores were used as outcome measures. For example: about a third of incident (32%) and of prevalent (36%) cases had reduced social functioning for four years or more. Incident cases are those with the onset of illness two years or less on entry to the study.

Table 3
Factors associated with long-term (11-year) social functioning of people with bipolar disorder in Butajira, Ethiopia.

		Incident cases[*]				Prevalent cases				All cases			
		B[**]	95% confidence interval		P	B[**]	95% confidence interval		P	B[**]	95% confidence interval		P
			Lower	Upper			Lower	Upper			Lower	Upper	
Age	Years	−.05	−.2	.1	ns	.01	−.04	.1	ns	.003	−.04	.04	ns
Sex	Female	.2	−1.4	1.7	ns	.3	−.4	1.1	ns	.3	−.4	.9	ns
	Male	Ref				Ref				Ref			
Residence	Urban	.3	−2.4	2.9		.01	−1.0	1.0		.1	−.9	1.0	
	Other	Ref			ns	Ref			ns	Ref			ns
Education	Years	−.05	−.4	.3		−.1	−.2	.1		−.1	−.2	.1	
Religion	Muslim	.9	−1.2	2.9	ns	−.7	−1.5	.1	ns	−.6	−1.3	.2	ns
	Other	Ref				Ref				Ref			
Marital status	Married	.4	−1.8	2.6	ns	−.6	−1.5	.3	ns	−.5	−1.3	.3	ns
	Other	Ref				Ref				Ref			
Age of onset	Years	−.1	−1.2	.9		.01	−.1	.1		−.001	−.1	.1	
					ns				ns				ns
Speed of onset	Acute	−.3	−3.6	3.0		.02	−2.0	2.0		.1	−1.6	1.8	
	Insidious	Ref				Ref				Ref			
Duration of illness at entry	Years	.02	−.2	.2	ns	.01	−.1	.1	ns	.01	−.04	.1	ns
Baseline history of treatment	No	2.8	−1.2	6.8	ns	1.0	−1.5	3.5	ns	1.4	−.7	3.5	ns
	Yes	Ref											
Medication adherence	≤75%	.3	−1.6	2.2	ns	−.5	−1.2	.2	ns	−.4	−1.1	.2	ns
	> 75%	Ref											
					ns				ns				ns
Substance use	No	−1.0	−3.2	1.1		.5	−.8	1.7		.1	−.9	1.2	
	Yes	Ref				Ref				Ref			
Follow-up mania symptom severity score	1–6	.03	−.9	1.0	ns	−.1	−.6	.4	ns	−.04	−.5	.4	ns
Follow-up depression symptom severity score	1–6	.1	−1.1	1.3	ns	.1	−.3	.5	ns	.1	−.3	.5	ns
Baseline social function score	1–100	.4	.3	.5	< 0.001	.5	.4	.5	< 0.001	.5	.4	.5	< 0.001
Time	Years	1.5	.7	2.3	< 0.001	1.6	1.2	2.0	< 0.001	1.6	1.2	1.9	< 0.001
Intercept	1–100	74.3	69.8	78.7	< 0.001	72.7	70.6	74.9	< 0.001	73.1	71.1	75.0	< 0.001

* Incident cases are those with the onset of illness two years or less on recruitment to the study.

** Yearly follow-up mean scores on the Short Form Medical Outcome (SF-36) social function scores were used as outcome measures. Coefficients, B, obtained from a random coefficient model adjusted for age, sex, baseline SF36 scores, longitudinal PSR scores, and follow-up duration. A positive coefficient, B, indicates a trend of improvement in functioning. ns = not significant.

mental health literacy. Our report of the lack of significant association of improved functional outcome with the duration of illness and history of medical treatment at baseline may not correspond to reports of other studies (Altamura et al., 2011; Medeiros et al., 2016Medeiros, Senco, Lafer, & Almeida, 2016; Vieta et al., 2018). Again, comparison of our findings with what has been reported in the literature may be difficult because of methodological differences.

As was the case in the present study, depressive symptoms were not associated with functional outcome when adjusted for demographic and clinical characteristics, in the Systematic Treatment Enhancement Program for BD (STEP-BD) Study (Zhang et al., 2006). However, other studies had shown such relationship as reviewed by (Gitlin & Miklowitz, 2017), which showed a large percentage of cases continued to have lower functioning even when they were not symptomatic, and the poor functioning in BD was due more to depressive symptoms than mania. It is not clear whether such associations persist on the long-term as almost all of these studies were cross-sectional or short-term (Kennedy, Foy, Sherazi, McDonough, & McKeon, 2007) and did not adjust for baseline functioning in their analyses as we did. Most of the effect of symptom severity could be early in the follow-up period as was the case in the present study. In our earlier study of short-term functioning (Fekadu et al., 2006; Kebede et al., 2006) symptoms were significantly associated with functional outcome in the short-term. Our study, however, examined the role of symptom severity on functional improvement during follow-up for an average of 11 years. It is also possible that discrimination, which was not measured in the present study, was associated with functional outcome, independent of symptom severity – for example those that have achieved full

symptomatic recovery may have difficulty getting a job or getting married because of their previous behavior when symptomatic (Habtamu, Alem, & Hanlon, 2015).

There are some limitations to this study. One of the limitations of the study is that the prevalence of MDD reported in the current study is lower than expected from the literature, including our previous report (Kebede & Alem, 1999) of the prevalence of 3.4% in females and 1.4% in males. In their systematic review of global variations of the prevalence of MDD, Ferrari, Somerville, et al. (2013), had reported a global average of 4.7%. The reason for the lower prevalence of MDD in our study, and whether this sample is an unbiased selection, is thus not clear. It is possible that cases of MD with psychotic features were over-represented in the sample because the identification and recruitment of cases of MDD were done together with that of schizophrenia and BD. The psychotic features of the latter two diagnoses and our use of key informants to identify cases from the community may have resulted in a preferential selection of cases MDD with psychotic features, although we cannot confirm this given the present data. We have not assessed cognitive deficits, which have been shown to be strongly associated with functioning (Gitlin & Miklowitz, 2017). We were not able to do more frequent assessments of functional outcomes for logistic reasons, and thus, cannot ascertain whether our yearly outcome assessments truly reflect the pattern of outcome for the whole 12 months between assessment.

In conclusion, our study shows that the levels of functioning of both people with BD and MDD were significantly lower than that of the general population at baseline and follow-up. Although there were improvements in function with follow-up, between a third of people

Table 4
Factors associated with long-term (11-year) social functioning of people with major depressive disorder in Butajira, Ethiopia.

		Incident cases[*]				Prevalent cases				All cases			
		B[**]	95% confidence interval		P	B[**]	95% confidence interval		P	B[**]	95% confidence interval		P
			Lower	Upper			Lower	Upper			Lower	Upper	
Age	Years	−.02	−.1	.1	ns	.02	−.03	.1	ns	.01	−.03	.1	ns
Sex	Female	−.2	−2.2	1.7	ns	.4	−.6	1.3	ns	.2	−.6	1.1	ns
	Male	Ref				Ref				Ref			
Residence	Urban	2.0	−.4	4.4	ns	1.1	−.1	2.4	ns	1.3	.2	2.4	ns
	Other	Ref				Ref				Ref			
Education	Years	.4	−.004	.8	ns	.1	−.2	.3	ns	.2	−.01	.4	ns
Religion	Muslim	−1.5	−3.8	.8	ns	−.1	−1.0	.9	ns	−.3	−1.2	.6	ns
	Other	Ref				Ref				Ref			
Marital status	Married	.2	−1.8	2.2	ns	.8	−.4	1.9	ns	.7	−.3	1.7	ns
	Other	Ref				Ref				Ref			
Age of onset	Years	.3	−1.0	1.6	ns	.01	−.1	.1	ns	−.001	−.1	.1	ns
Speed of onset	Acute	.9	−1.6	3.4	ns	−.2	−1.5	1.2	ns	−.1	−1.3	1.0	ns
	Insidious	Ref				Ref				Ref			
Duration of illness at entry	Years	−.2	−1.4	1.1	ns	.1	−.002	.1	ns	.1	.001	.1	ns
Baseline history of treatment	No	−2.3	−7.0	2.4	ns	−1.9	−5.9	2.1	ns	−2.1	−5.0	.8	ns
	Yes	Ref				Ref				Ref			
Medication adherence	≤75%	−1.4	−3.8	.9	ns	.8	−.1	1.8	ns	.4	−.4	1.3	ns
	> 75%	Ref				Ref				Ref			
Substance use	No	−3.7	−8.7	1.4	ns	−1.9	−4.1	.2	ns	−2.2	−4.1	−.2	ns
	Yes	Ref				Ref				Ref			
Follow-up symptom severity score	1–6	.2	−.6	1.0	ns	.2	−.2	.7	ns	.1	−.3	.5	ns
Baseline social function score	1–100	.6	.4	.8	< 0.001	.5	.4	.6	< 0.001	.5	.5	.6	< 0.001
Time	Years	1.8	.7	2.9	0.001	1.9	1.3	2.4	< 0.001	1.9	1.4	2.4	< 0.001
Intercept	1–100	68.9	63.5	74.4	< 0.001	68.2	65.2	71.2	< 0.001	68.4	65.8	71.0	< 0.001

[*] Incident cases are those with the onset of illness two years or less on recruitment to the study.

[**] Yearly follow-up mean scores on the Short Form Medical Outcome (SF-36) social function scores were used as outcome measures. Coefficients, B, obtained from a random coefficient model adjusted for age, sex, baseline SF36 scores, longitudinal PSR scores, and follow-up duration. A positive coefficient, B, indicates a trend of improvement in functioning. ns = not significant.

with BD and half of MDD cases had functional deficits in the long-term. When baseline functioning was controlled for, none of the demographic or clinical characteristics of cases were associated with longitudinal functioning.

Conflict of interest

None declared.

Ethical statement

The study was approved by the ethical review committees of both the Department of Community Health and the Faculty of Medicine, Addis Ababa University. The study has made possible the establishment of a mental health service in the district. The people identified with BD or MDD were offered psychiatric treatment as appropriate, free of charge and this has continued until the present.

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